REMARKS

Claims 35-54 and 69 were pending in this application. No claims are canceled and no claims added. Thus, after entry of this amendment, **claims 35-54 and 69 will still be pending**.

Claim 69 is amended to correct an inadvertent error in a sequence identifier. No new matter has been added to the claims.

EXAMINER INTERVIEW

Applicant thanks Examiner Parkin for the courtesy of a telephone interview with Applicant's representatives Tanya M. Harding and Jodi L. Connolly on May 30, 2007. During the interview, the pending rejections under 35 U.S.C. §103(a) were discussed. The Examiner maintained that the claimed subject matter is *prima facie* obvious in view of the cited references. However, the Examiner indicated that a Declaration by the inventor demonstrating unexpected superior results may be sufficient to overcome the rejections. Therefore, provided herewith is a Declaration under 37 C.F.R. §1.132 by inventor Gwong-Jen J. Chang.

INFORMATION DISCLOSURE STATEMENT

Applicant notes that the Information Disclosure Statement (IDS) mailed March 15, 2004, and date-stamped by OIPE March 18, 2004, has not been indicated to be considered by the Examiner. Applicant respectfully requests that the IDS be considered and the cited references be made of record in the application, and that a signed copy of the Form 1449 be provided with the next Office action.

REJECTIONS UNDER 35 U.S.C. §103(a)

Claims 35-37, 39-45, 47-49, 51-54 and 69 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Phillpotts *et al.* (1996) in view of Kozak (1987). The Office argues that Phillpotts *et al.* disclose a transcriptional unit comprising the St. Louis encephalitis virus prM/E gene, which includes the prM signal sequence, the cytomegalovirus major immediate-early promoter and a polyA terminator sequence. The Office further alleges that since Kozak teaches the optimal sequence for eukaryotic translational initiation, it would have been obvious to include the Kozak consensus sequence in the transcriptional unit taught by Phillpotts *et al.*

Claims 38, 46 and 50 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Phillpotts *et al.* (1996) in view of Kozak (1987) and Konishi *et al.* (1992). The Office alleges Konishi *et al.* teach that co-expression of prM/E of Japanese encephalitis virus results in the production of subviral particles, which are highly immunogenic. Therefore, the Office concludes one of skill in the art would have reasonably expected co-expression of the prM/E genes to produce highly immunogenic subviral particles. Applicant traverses both of these rejections.

Applicant maintains that the claims are not *prima facie* obvious in view of the cited references for the reasons of record (see the Amendment and Response filed September 13, 2006). However, solely in an effort to advance prosecution of the application, submitted herewith is a Declaration under 37 C.F.R. §1.132 by inventor Gwong-Jen J. Chang, which establishes that the claimed transcriptional units exhibit unexpected superior results over the cited art.

As detailed in the Declaration, the flavivirus vaccine constructs described in the specification that comprise the claimed transcriptional units exhibit unexpectedly superior results over any teachings in the cited art, and over other previously described flavivirus constructs. Even a single dose of the flavivirus constructs described in the instant application (for example, pCDJE2-7, pCBJE1-14 and pCIBJES14) results in 100% protection against subsequent flavivirus challenge, elicits significant production of neutralizing antibody, and confers passive protection by maternal antibody. In contrast, previously described flavivirus vaccine constructs, which also comprise the prM signal sequence, prM/E, the CMV immediate early (IE) promoter and a polyA terminator, but lack a Kozak signal sequence, do not confer complete protection against flavivirus challenge, and do not result in the production of significant, if any, neutralizing antibody. For example, administration of the St. Louis encephalitis virus (SLEV) construct described by Phillpotts *et al.* results in no more than 75% protection against virus challenge, and does not result in the production of neutralizing antibody. pJME, a Japanese encephalitis virus (JEV) vaccine construct described by Lin *et al.* (*J. Virol. 72(1)*:191-200, 1998)[1] results in only 70% protection against lethal challenge and elicits little to no neutralizing antibody.

Furthermore, a JEV vaccine construct described by Konishi *et al.* (*J. Virol. 72(6)*:4925-4930, 1998),[1] which comprises prM/E, the CMV IE promoter, a polyA terminator and a Kozak sequence

[1] Copies of Lin *et al.* and Konishi *et al.* were provided with the Information Disclosure Statement dated March 5, 2001.

(CGAATTCACC) that differs from the claimed ribosomal binding sequence (GCCGCCGCC), only confers up to 90% protection against flavivirus challenge when administered at the highest dose tested. In addition, the Konishi *et al.* construct does not elicit significant titers of neutralizing antibody.

Despite previous teachings in the art of different Kozak consensus sequences, Dr. Chang, the sole inventor of the application, specifically selected a ribosomal binding sequence comprising GCCGCCGCC, in combination with the prM signal sequence, for expression of high quantity and high quality (*e.g.*, highly immunogenic) flavivirus antigen. As disclosed in the specification and outlined in the Declaration, this combination resulted in unexpectedly superior results, exemplified by the findings that even a single dose of a vaccine comprising the claimed transcriptional units results in 100% protection against flavivirus challenge, even in mice as young as 3 days old; elicits significant production of neutralizing antibody; and confers passive protection by maternal antibody.

Therefore, the claimed transcriptional units are not obvious in view of the cited references. Accordingly, Applicant requests withdrawal of these rejections under 35 U.S.C. §103(a).

REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claim 69 is rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. The Office states that SEQ ID NO: 5 does not contain the nucleotide sequence GCCGCCGCCATGT, referenced in claim 69. In response, Applicants have amended claim 69 to properly identify SEQ ID NO: 13 as reciting the claimed nucleotides. Accordingly, Applicant requests withdrawal of this rejection under 35 U.S.C. §112, second paragraph.

CONCLUDING STATEMENT

Applicant believes that the foregoing comprises a full and complete response to the Office Action of record. Withdrawal of the pending rejection and allowance of the claims is respectfully requested. If the Examiner believes that there are any remaining issues in the case that could be resolved by a telephonic interview, the Examiner is encouraged to contact the representative for Applicant listed below to discuss any outstanding matters.

Respectfully submitted,

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